functional, whether by deletion or mutation, such that the adenovirus is incapable of replicating autonomously in the target cell

- page 9, lines 23-26 states in particular that the adenovirus lacks the sequences necessary for replication in the infected cell, i.e., the E1 region
- page 24, lines 9-13 describe cotransfecting the BDNF plasmid with a defective adenovirus vector in 293 helper cells, which provide E1 region functions in trans.

The limitation "defective recombinant adenovirus" in claim 27 clearly distinguishes the claimed vector from Barde. Applicants have further amended this claim to emphasize this distinction. Thus, contrary to the Examiner's contention, the claimed invention has a special technical feature and satisfies the criteria for unity of invention. The restriction requirement is improper and should be withdrawn.

Enablement of the Claimed Invention

The specification enables gDNA encoding BDNF

The Examiner has rejected claims 30 and 36 under 35 U.S.C. § 112, first paragraph, contending that genomic DNA encoding BDNF is not enabled. Applicants respectfully traverse this rejection, and wish to point out that the minimal recombinant adenovirus genome, containing the ITRs and encapsidation sequences (see the Specification at page 9, lines 12-17) permits introduction of 20-30 kilobases of heterologous DNA. Furthermore, inclusion of introns does not require any manipulation by the skilled artisan: the endogenous cellular splicing mechanisms operate to provide splicing of the transcript. Indeed, in eukaryotic cells, genomic DNA sequence are often expressed at a higher level, perhaps because they are translated through the endogenous pathways, including splicing.

Nevertheless, in order to advance prosecution of the instant application, Applicants have canceled claims 30 and 36 without prejudice. Applicants reserve the right to prosecute the subject matter of the canceled claims in a related application. Thus, the Examiner's rejection is moot and should be withdrawn.

The Specification enables BDNF

The Examiner has rejected claims 27-29, 31-34, 37-41, and 48-50 under 35 U.S.C. § 112, first paragraph, contending that the specification does not enable any substance or derivative that may be named "brain-derived neurotrophic factor."

In response, Applicants have amended the claims to recite "brain-derived neurotrophic factor (BDNF)", which the Examiner stated is enabled. One of ordinary skill in the art is fully enabled by this term for a molecule that has the chemical and structural characteristics to function as BDNF, e.g., as described in Barde.

In view of this amendment, the Examiner's rejection is obviated and should be withdrawn.

The Claimed Invention Is Novel

The Examiner has rejected claims 27-29, 31, and 48 under 35 U.S.C. § 102(b) as allegedly anticipated by Barde. Applicants traverse.

As noted above, Barde fails to teach a defective recombinant adenovirus vector, particularly a vector with a non-functional E1 region.

Anticipation under 35 U.S.C. § 102 requires identity of invention. Scripps Clinic & Research Fdn. v. Genentech Inc., 927 F.2d 1565, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991). Furthermore, "it is axiomatic that for prior art to anticipate under §102 it has to meet every element of the claimed invention." Hybritech v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986) (emphasis added). Barde is not identical with the claimed invention; it lacks the element of the claimed invention that the adenovirus vector is defective, i.e., the E1 region is non-functional. The present amendment has been made to emphasize this point.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection is overcome and should be withdrawn.

The Claimed Invention is Non-obvious

The Examiner has rejected claims 32-35, 37-41, and 48-50 under 35 U.S.C. § 103(a) as allegedly unpatentable over Barde in view of Le Gal La Salle (1993, Science 259:988-990). Applicants respectfully traverse this rejection.

For the reasons advanced above, Barde does not teach the claimed invention. In addition, Applicants have noted that the claimed subject matter is entitled to priority under 35 U.S.C. §§ 119, 120, and 365 of co-pending US Application Serial No. 08/403,868, filed April 28, 1995, which is the National Phase of PCT/EP93/02519, filed September 17, 1993, and of European Patent Application No. EP92-402644.6, filed September 25, 1992. Thus, the instant application is effectively a continuation-in-part of the above-noted priority applications. Thus, with an effective US filing date of September 1993, and a priority date of September 1992, Le Gal La Salle is not available as prior art to the instant application.

Furthermore, even if Le Gal La Salle were available, there is not hint or suggestion contained in this reference to express BDNF in an adenovirus vector. In particular, Barde does not suggest, much less teach, methods of gene therapy. Thus, there is no suggestion, save that found by application of hindsight gained from the instant disclosure, of the claimed vector which is engineered for expression in cells of the central nervous system, particularly in nerve cells. Indeed, the teaching in Barde is of protein therapy, which leads away from the claimed invention and from the combination with La Gal La Salle. Moreover, this latter references does not teach or suggest expression of BDNF, or of any advantages to be gained from expression of this gene in vivo in cells of the central nervous system, in particularly nerve cells.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's rejection is overcome and should be withdrawn.

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